Appl. No. 10/815,468
Amdt. dated July 20, 2006
Amendment under 37 CFR 1.116 Expedited Procedure
Examining Group 1641

PATENT

REMARKS/ARGUMENTS

Upon entry of the present amendment, claims 1-7, 12-13 and 29-30 are pending in the application and presented for examination. Claims 2-7 are unchanged from the original claims as filed, Claims 12 and 13 are previously presented, Claims 9-10 and 14-28 are withdrawn, Claims 1, 29 and 30 are currently amended and Claims 8 and 11 are canceled and the subject matter of these claims has been incorporated into claims 1, 29 and 30. Applicant submit that no new matter is present in this or any other portion of the present amendment. Reconsideration of the application is respectfully requested in view of the amendment to the claims and the accompanying remarks.

I. REJECTIONS UNDER 35 U.S.C. §102

Claims 1-3, 6-7, and 29-30 stand rejected under 35 U.S.C. 102(e) over U.S. Patent No. 6,704,104 to Li (hereinafter "Li") and Claims 1, 4-6, and 29-30 stand rejected under 35 U.S.C. 102(b) over U.S. Patent No. 6,489,159 to Chenchik *et al.* (hereinafter "Chenchik *et al.*"). While not acquiescing to the Patent Office's position and solely to expedite the prosecution of important subject matter, Applicants have amended claims 1, 29 and 30 to incorporate the limitations of claim 8, which is not subject to the rejection. In view of the amendment, Applicants believe that the rejections under 35 U.S.C. 102 are rendered moot. Notwithstanding the amendment, the Applicants point out the differences between the cited references and the presently claimed invention in Section II below, so as not to prejudice future prosecution of this subject matter in a subsequent continuation or divisional application.

II. REJECTIONS UNDER 35 U.S.C. §103(a)

Claim 8 stands rejected as allegedly being obvious over Li *et al.* in view of U.S. Patent Publication No. 2003/0073157 to Bertozzi *et al.* (hereinafter "Bertozzi *et al.*") and claims 11-13 stand rejected as allegedly being obvious over Chenchik *et al.* The Examiner alleges that Li and Bertozzi *et. al.* and Chenchik *et al.* teach a microarray wherein the ligand concentration in

each discrete region is normalized as was claimed in the instant application. Insofar as the rejection is applicable to the amended claim set, Applicants respectfully traverse the rejection.. While the applicants note that only dependent claims 8 and 11-13 were rejected, the analysis herein is also applicable to the claims from which they depend.

To render obvious a pending claim, a prior art reference must provide all limitations of the claim. MPEP §2143:

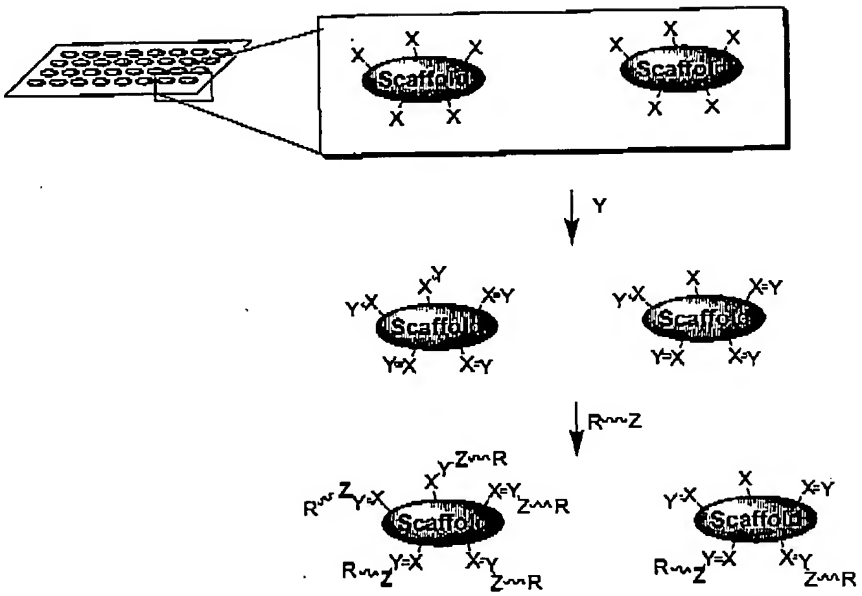
> [t]o establish a *prima facie* case of obviousness, *three* basic criteria must be met. *First*, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *Second*, there must be a reasonable expectation of success. *Finally*, the prior art reference (or references when combined) *must teach or suggest all the claim limitations*. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure.

As set forth herein, the alleged prior art references do not teach or suggest all the claim limitations and thus, a *prima facie* case of obviousness of the claims has not been established. The confusion on the part of the Patent Office appears to center on the different use of the term "normalize" in Li, Chenchik and the present application. Li and Chenchik *et al.* disclose either of two standard methods to prepare their ligand-microarrays which were well known in the art (*see* also Lam and Renil, *Current Opinion in Chemical Biology*, 2002, 6: 353-8, attached as Exhibit A).

As illustrated in Figure 1, the first method involves the *in situ* synthesis of ligands on a scaffold on the support. Using this method it is difficult to obtain a ligand microarray with substantially normalized molar concentration of ligand on each spot because of incomplete reactions at each synthetic step.

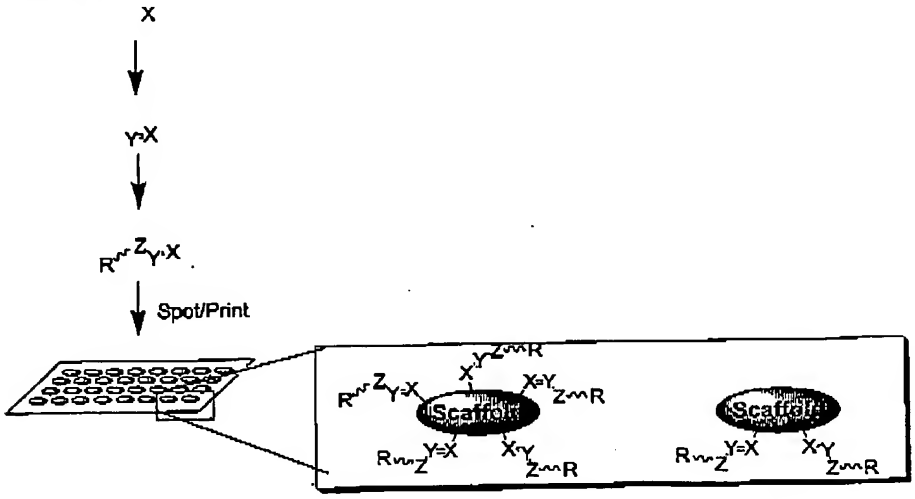
Figure 1

Appl. No. 10/815,468
Amdt. dated July 20, 2006
Amendment under 37 CFR 1.116 Expedited Procedure
Examining Group 1641



As illustrated in Figure 2, the second method involves presynthesizing the ligands and then chemically ligating the ligands onto a scaffold on the support. This can be done via chemo-selective or non-specific ligation, but by either method it is difficult to control reactivity to obtain a ligand array with substantially normalized molar concentration of ligand in each spot.

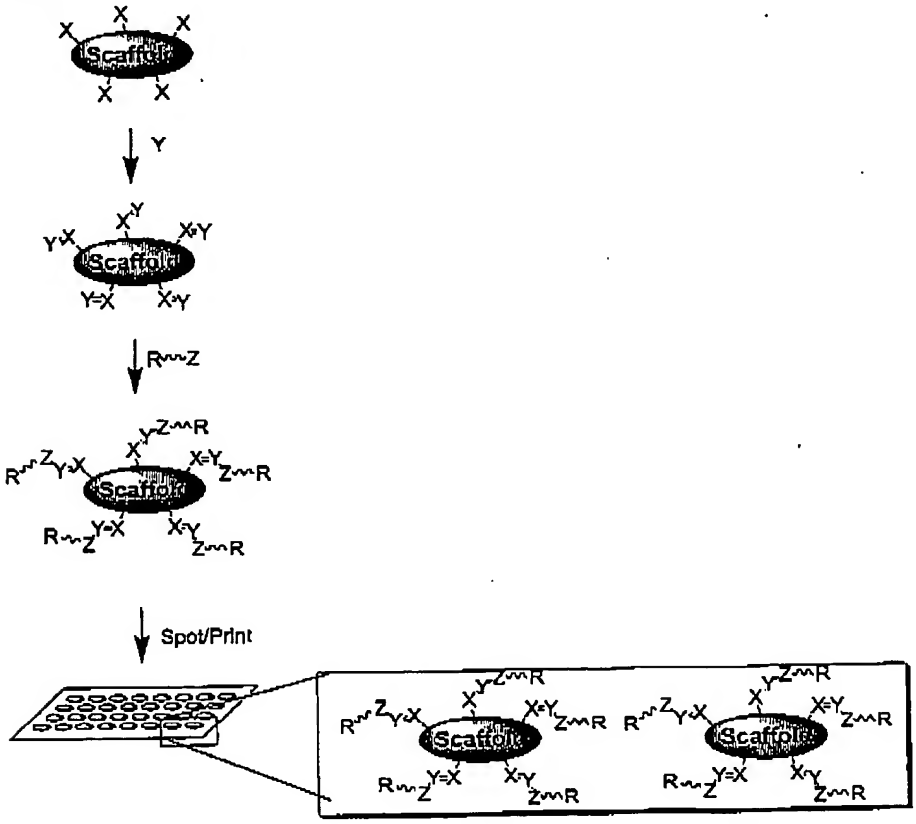
Figure 2.



Appl. No. 10/815,468
Amdt. dated July 20, 2006
Amendment under 37 CFR 1.116 Expedited Procedure
Examining Group 1641

The present invention is directed toward a microarray wherein the molar concentration of ligand attached to the biopolymer scaffold in each discrete region of the microarray is substantially normalized, or as the amended claims now read: ***the concentration of ligand in each discrete region of the microarray varies less than 50%***. This refers to the ***physical concentration*** of ligand in each discrete region of the microarray. This novel and unobvious feature of the invention is illustrated in Figure 3. The differences between the cited art and the present invention are readily apparent by examining the way that the presently claimed microarray is synthesized.

Figure 3.



Using the chemoselective methods disclosed in the present application, initially reacting the scaffold with an excess amount of ligand enables one to control and equalize the concentration of conjugated ligand per scaffold, resulting in a ligand-scaffold ratio which can be identical between conjugated scaffolds. Further, the amount of scaffold to spot can be controlled through chemoselective ligation. In this way, the product microarray will have substantially equal molar concentration of ligand in each spot. This feature of normalized molar concentration of ligands is very difficult, if not impossible, to obtain with the previously disclosed methods, (*see* Xu *et al Molecular Diversity* 2004, 8:301-10, attached as Exhibit B).

Li discloses microarrays of Figure 1 and 2 and then uses ***optical*** methods of his plate reader to "normalize" the resulting data from a site on the array. The method does disclosed microarrays with ***physically*** normalized concentrations of ligand in each spot. Applicants respectfully assert Li does not teach or suggest the presently claimed invention of a microarray comprising, *inter alia*, a support having a plurality of discrete regions having a ligand modified-biopolymer spotted thereon, ***wherein the physical concentration of the ligand in each discrete regions of the microarray varies less than 50%.***

Similarly, Chenchik *et al.* discloses microarrays of Figure 1 and 2 wherein a reference housekeeping gene is incorporated in each mixture. The housekeeping gene is used to ***mathematically*** "normalize" the biopolymer concentration in each spot/ relative amounts of target composition in each spot (*see* column 13, lines 4-30 and 36-39). Chenchik *et al.* do not teach or suggest Applicants' claimed microarray wherein the actual ***physical concentration*** of the ligand in each discrete regions of the microarray varies less than 50%.

Bertozzi et al. simply discloses the use of chemo-selective ligation to generate a peptide-conjugate. Bertozzi et al. do not cure the deficiencies of Li or Chenchik *et al.* as they do not mention ligand concentration and therefore it cannot teach or suggest that the ligand concentration is within a particular range. Applicants submit that the limited teaching of Bertozzi would also fail to motivate one skilled in the art to prepare any arrays in which ligand concentration is normalized or within a particular range. In the absence of any direction in Bertozzi, Applicants submit that the cited references do not teach or suggest the claimed features ,

of the present invention and respectfully request that the present rejection under 35 U.S.C. §103(a) be withdrawn and send this application to issue.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

Mark H. Hopkins, Ph.D.
Reg. No. 44,775

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300

Attachments
M3H:lls
60826381 v1